PATENT COOPERATION TOTAL

From the

INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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York House
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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing (day/month/year)

1 0.05.99

Applicant's or agent's file reference

P1066P2

International filing date (day/month/year)

30/01/1998

Priority date (day/month/year) 07/02/1997

IMPORTANT NOTIFICATION

Applicant

GENENTECH, INC. et al.

International application No.

PCT/US98/01774

- 1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- 2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

Authorized officer

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| Applicant's o | or ager | nt's file reference | | See Notification of | of Transmittal of Internation | |
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| P1066P2 | _ | | FOR FURTHER ACTION | | nination Report (Form PCT | |
| International | applic | eation No. | International filing date (day/monti | n/year) Prio | rity date (day/month/year) | |
| PCT/US9 | | | 30/01/1998 | į. | 02/1997 | |
| Internationa C12N15/ | | nt Classification (IPC) or na | tional dassification and IPC | | | |
| Applicant | | | | | | |
| GENENT | ECH, | INC. et al. | | | | |
| | | tional preliminary exami mitted to the applicant a | ination report has been prepare according to Article 36. | d by this Internation | onal Preliminary Examir | ning Authority |
| 2. This F | EPOI | RT consists of a total of | 5 sheets, including this cover s | heet. | | |
| be (s | een ar ee Ru | nended and are the bas | d by ANNEXES, i.e. sheets of the sis for this report and/or sheets of the of the Administrative Instruct a sheets. | containing rectification | ations made before this | hich have Authority |
| 3. This r | | contains indications rela | ating to the following items: | - | | |
| 11 | _ | Priority | | | | |
| 111 | \boxtimes | Non-establishment of c | ppinion with regard to novelty, in | ventive step and i | industrial applicability | |
| IV | | Lack of unity of invention | | | | |
| V | M | | nder Article 35(2) with regard to ons suporting such statement | novelty, inventive | e step or industrial appli | icability; |
| VI | | Certain documents cit | ed | | | |
| VII | | Certain defects in the i | nternational application | | | |
| VIII | ⊠ | Certain observations o | n the international application | | | |
| Date of sub | | n of the demand | Date of | f completion of this r | eport 1 0.05.99 | |
| Name and | mailing | address of the internation | al Author | ized officer | | (SOCIAL) |
| | exami | ning authority: | Addio | LUZ OMOU! | | Se |
| (O) | D-80 | pean Patent Office 298 Munich | | ach, S | | |
| | | (+49-89) 2399-0 Tx: 52365 (+49-89) 2399-4465 | · · | ono No. (+49-89) 22 | 000 0745 | SOUNDING FORCE |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US98/01774

| I. | Basis | of th | report |
|----|--------------|-------|--------|
|----|--------------|-------|--------|

| 1. | resp | oonse to an invitation | | referred to in this repo | | shed to the receiving Office led" and are not annexed to | |
|--------------|------|------------------------|--|--------------------------|--------------------|---|----|
| | Des | cription, pages: | | | | | |
| | 1-89 | 5 | as originally filed | | | | |
| | Cla | ims, No.: | · | | | | |
| | 1-22 | 2 | as received on | 23/12/1998 | with letter of | 21/12/1998 | |
| | Dra | wings, sheets: | | | | | |
| | 1/23 | 3-23/23 | as originally filed | | | | |
| 2. | The | amendments have | e resulted in the cancell | lation of: | | | |
| | | the description, | pages: | | | | |
| | | the claims, | Nos.: | | | | |
| | | the drawings, | sheets: | | | | |
| 3. | | | een established as if (so beyond the disclosure a | | | made, since they have bee | ∍n |
| 4. | Add | litional observation | s, if necessary: | | | | ₹1 |
| 1 ((. | . No | n-establishment o | of opinion with regard | to novelty, inventive | step and indust | trial applicability | |
| | | | ne claimed invention app cable have not been exa | | nvolve an inventiv | ve step (to be non-obvious) | ١, |
| | | the entire internat | tional application. | | | | |
| | Ø | claims Nos. 10. | | | | | |
| | | | | | | | |

because:

INTERNATIONAL PRELIMINARY **EXAMINATION REPORT**

International application No. PCT/US98/01774

| | | the said international ap not require an internation | | | aid claims Nos. relate to the following subject matter which does xamination (specify): |
|----|------|---|-------------|------------------|---|
| | ⊠ | that no meaningful opini | | | rate particular elements below) or said claims Nos. 10 are so unclea ed (specify): |
| | | see separate sheet | | | |
| | | the claims, or said claim could be formed. | ıs Nos. | are so in | adequately supported by the description that no meaningful opinion |
| | | no international search i | report h | as been e | established for the said claims Nos |
| ٧. | | | | | ith regard to novelty, inventive step or industrial upporting such statement |
| 1. | Sta | tement | | | |
| | Nov | velty (N) | Yes: No: | Claims Claims | 2,3, 1,4-9,11-22 |
| | Inv | entive step (IS) | Yes: No: | Claims Claims | 2,3, |
| | Ind | ustrial applicability (IA) | Yes: No: | Claims Claims | 1-22 |
| 2. | Cita | ations and explanations | | | |

2.

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

- 1. The present application relates to a new substrate protein (PSTPIP) for the known PST HSCF thyrosine phosphatase, an antagonist of said PSTPIP polypeptide, an antibody and methods for its production and use.
- None of the cited documents discloses or suggest the specific PSTPIP 2. polypeptide. Therefore the present application is considered to contain patentable subject-matter.
- However, the following objections apply to present set of claims. The claims are not restricted to the specific protein for which novelty and inventiveness is acknowledged. Instead the claims in its broadest sense also cover functional derivatives of said protein. The definition "peptides encoded by nucleic acid which hybridizes under stringent conditions to nucleic acid shown in Seq. D No:1 provided that it retains the ability to bind to a PEST-type protein thyrosine phosphatase" embraces e.g. the CDC15p a Schizosaccharomyces pombe phosphoprotein cited in the description of the present application, as well as the p130cas protein from Hela cells which is disclosed in D1: Molecular and Cellular Biology, vol. 16, No. 11, 1996). Therefore claim 1 contains subject-matter not allowed under Article 33(2) PCT.

The same objection also apply to present claims 4,5-9. Since the nucleic acid claims, the antibody claims and the method claims refer back to the protein claims the same

lack of novelty objection also apply to said claims (present claims 11-18, 19-22).

Moreover, claim 10 which relates to an antagonist of PSTPIP is objectionable under Article 6 PCT because said claim is totally unclear. Without any technical features defining the antagonist, said antagonist can also be a known compound. Therefore, before an examination with regard to said claim can be carried out the antagonist need

4. In summary, the present claims are broadened in a manner that non-novel subject-matter is embraced by said claims.

When drafting new claims, the following vague expressions should be avoided: The vague definition used in claim 1 item (iii) is unclear and thus objectionable under Article 6 PCT.

5. The applicant is informed that if the priority claimed in the present application is

to be specified.

INTERNATIONAL PRELIMINARY **EXAMINATION REPORT - SEPARATE SHEET**

novelty of the claims.

International application No. PCT/US98/01774

not valid, an intermediate document becomes highly relevant for the assessment of

Claims:

1. An isolated PSTPIP polypeptide selected from the group consisting of:

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(i) a polypeptide comprising the amino acid sequence
 of the PSTPIP polypeptide shown in Fig. 1A (SEQ
 ID NO:1);

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(ii) a polypeptide having at least 65% sequence homology with the PSTPIP amino acid sequence of Fig. 1A (SEQ ID NO:1); and

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(iii) a polypeptide encoded by nucleic acid which
 hybridizes under stringent conditions to nucleic
 acid encoding the polypeptide of (i);

20

provided that the polypeptides of (ii) and (iii) substantially retain the ability to bind to a member of the PEST-type protein tyrosine phosphatases.

2. The PSTPIP polypeptide of Claim 1 having at least 85% sequence homology with the PSTPIP amino acid sequence of Fig. 1A (SEQ ID NO:1).

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3. The PSTPIP polypeptide of Claim 1 comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig 1A (SEQ ID NO:1).

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4. The PSTPIP polypeptide of Claim 1 which is capable of being dephosphorylated by a member of the PEST-type protein tyrosine phosphatases when phosphorylated on at least one tyrosine residue.

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5. The PSTPIP polypeptide of Claim 1, wherein the member of the PEST-type protein tyrosine phosphatases is PTP HSCF.

- 6. The PSTPIP polypeptide of Claim 1 which is devoid of a C-terminal SH3 domain.
- 7. The PSTPIP polypeptide of Claim 1 which is not phosphorylated.
 - 8. The PSTPIP polypeptide of Claim 1 which is phosphorylated on at least one tyrosine residue.
- 10 9. The PSTPIP polypeptide of Claim 1 which associates with actin.
 - 10. An antagonist of the PSTPIP polypeptide of Claim 1.
- 15 11. An isolated nucleic acid sequence which encodes the PSTPIP polypeptide of Claim 1.
- 12. A vector comprising the nucleic acid sequence of Claim
 11 operably linked to control sequences recognised by a
 20 host cell transformed with the vector.
 - 13. A host cell comprising the nucleic acid sequence of Claim 11.
- 25 14. A host cell comprising the vector of Claim 12.
 - 15. An antibody capable of specific binding to the PSTPIP polypeptide of Claim 1.
 - 30 16. The antibody of Claim 15 which is detectably labeled.
 - 17. The antibody of Claim 15 which is a monoclonal antibody.
 - 18. A hybridoma cell line which produces the antibody of35 Claim 15.
 - 19. A method for producing the PSTPIP polypeptide of Claim 1

comprising transforming a host cell with nucleic acid encoding said polypeptide, culturing the transformed cell and recovering said polypeptide from the cell culture.

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1 J. 18

- 20. A method for inducing the polymerization of actin monomers in a eukaryotic cell comprising introducing into said cell the PSTPIP polypeptide of Claim 1.
- 10 21. The method of Claim 20, wherein the step of introducing comprises introducing into said cell the vector of Claim 13.
- 22. An assay for identifying an antagonist or agonist of the PSTPIP polypeptide of Claim 1 which comprises contacting the PSTPIP polypeptide of Claim 1 with a candidate antagonist or agonist and monitoring the ability of said polypeptide to induce the polymerization of actin monomers.

PATENT COOPERATION TREATY



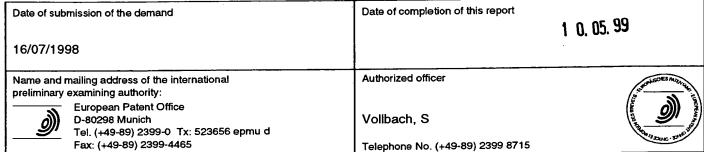
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

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| Applicant's or | agent's file reference | | See Notific | ation of Transmittal of International | | |
|------------------------------|--|--|----------------|---|--|--|
| P1066P2 | | FOR FURTHER ACTION | Preliminary | Examination Report (Form PCT/IPEA/416) | | |
| International a | pplication No. | International filing date (day/month | /year) | Priority date (day/month/year) | | |
| PCT/US98 | PCT/US98/01774 30/01/1998 07/02/1997 | | | | | |
| International F C12N15/12 | Patent Classification (IPC) or n | ational classification and IPC | | | | |
| Applicant | | | | | | |
| GENENTE | CH, INC. et al. | | | | | |
| 1. This into | ernational preliminary exar ransmitted to the applicant | nination report has been prepared according to Article 36. | d by this Inte | ernational Preliminary Examining Authority | | |
| 2. This RE | PORT consists of a total c | f 5 sheets, including this cover s | heet. | | | |
| bee (se | en amended and are the ba | asis for this report and/or sheets of 607 of the Administrative Instructi | containing re | on, claims and/or drawings which have ectifications made before this Authority he PCT). | | |
| 3. This rep | ☑ Basis of the report☐ Priority | lating to the following items: | | | | |
| UI | | opinion with regard to novelty, in | ventive step | and industrial applicability | | |
| IV | ☐ Lack of unity of invent | | 14 I | anthus at an arrindustrial applicability: | | |
| V | Reasoned statement citations and explanat | under Article 35(2) with regard to tions suporting such statement | noverty, inv | entive step or industrial applicability; | | |
| VI | ☐ Certain documents c | ited | | | | |
| VII | $\hfill\Box$ Certain defects in the | international application | | | | |
| VIII | ☐ Certain observations | on the international application | | | | |
| | | | | | | |
| Date of subm | ission of the demand | Date of | completion of | f this report | | |



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US98/01774

| 1. | Basis | of the | report |
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|----|--------------|--------|--------|

| 1. | resp | onse to an invitation | rawn on the basis of (<i>substitu</i> on under Article 14 are referre o not contain amendments.): | te sheets which d to in this repo | have been furnished rt as "originally filed" a | to the receiving Office in and are not annexed to |
|----------|---------------|---|--|--|---|--|
| | Des | cription, pages: | | | | |
| | 1-85 | 5 | as originally filed | | | |
| | Clai | ms, No.: | | | | |
| | 1-22 | 2 | as received on | 23/12/1998 | with letter of | 21/12/1998 |
| | Dra | wings, sheets: | | | | |
| | 1/23 | 3-23/23 | as originally filed | | | |
| 2. | The | amendments have | e resulted in the cancellation o | of: | | |
| | | the description, | pages: | | | |
| | | the claims, | Nos.: | | | |
| | | the drawings, | sheets: | | | |
| 3. | | This report has be considered to go I | een established as if (some of beyond the disclosure as filed |) the amendme I (Rule 70.2(c)): | nts had not been mad | e, since they have been |
| 4. | Ado | litional observation | s, if necessary: | | | |
| 111 | . Noi | n-establishment o | f opinion with regard to nov | relty, inventive | step and industrial | applicability |
| Tł or | ne qu to b | estions whether the industrially applic | e claimed invention appears t able have not been examined | to be novel, to in d in respect of: | nvolve an inventive st | ep (to be non-obvious), |
| | | the entire internat | ional application. | | | |
| | Ø | claims Nos. 10. | | | | |
| h. | | | | | | |

INTERNATIONAL PRELIMINARY **EXAMINATION REPORT**

International application No. PCT/US98/01774

| | | the said international ap not require an internatio | plicatior nal prel | n, or the s iminary e | aid claims Nos. relate to the following subject matter which does xamination (<i>specify</i>): |
|----|-------|--|-----------------------|--------------------------|--|
| | ⊠ | the description, claims of that no meaningful opini | | | rate particular elements below) or said claims Nos. 10 are so unclear ed (specify): |
| | | see separate sheet | | | |
| | | the claims, or said claim could be formed. | ıs Nos. | are so in | adequately supported by the description that no meaningful opinion |
| | | no international search | report h | as been e | established for the said claims Nos |
| | app | | | | ith regard to novelty, inventive step or industrial upporting such statement |
| | Nov | velty (N) | Yes: No: | Claims Claims | 2,3, 1,4-9,11-22 |
| | Inv | entive step (IS) | Yes: No: | Claims Claims | 2,3, |
| | Ind | ustrial applicability (IA) | Yes: No: | Claims Claims | 1-22 |
| 2. | Cita | ations and explanations | | | |
| | see | e separate sheet | | | |
| VI | II. C | ertain observations on t | the inte | rnationa | l application |

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

INTERNATIONAL PRELIMINARY InterEXAMINATION REPORT - SEPARATE SHEET

- 1. The present application relates to a new substrate protein (PSTPIP) for the known PST HSCF thyrosine phosphatase, an antagonist of said PSTPIP polypeptide, an antibody and methods for its production and use.
- 2. None of the cited documents discloses or suggest the specific PSTPIP polypeptide. Therefore the present application is considered to contain patentable subject-matter.
- 3. However, the following objections apply to present set of claims. The claims are not restricted to the specific protein for which novelty and inventiveness is acknowledged. Instead the claims in its broadest sense also cover functional derivatives of said protein. The definition "peptides encoded by nucleic acid which hybridizes under stringent conditions to nucleic acid shown in Seq. D No:1 provided that it retains the ability to bind to a PEST-type protein thyrosine phosphatase" embraces e.g. the CDC15p a Schizosaccharomyces pombe phosphoprotein cited in the description of the present application, as well as the p130cas protein from Hela cells which is disclosed in D1: Molecular and Cellular Biology, vol. 16, No. 11, 1996). Therefore claim 1 contains subject-matter not allowed under Article 33(2) PCT. The same objection also apply to present claims 4,5-9. Since the nucleic acid claims, the antibody claims and the method claims refer back to the protein claims the same lack of novelty objection also apply to said claims (present claims 11-18, 19-22).

Moreover, claim 10 which relates to an antagonist of PSTPIP is objectionable under Article 6 PCT because said claim is totally unclear. Without any technical features defining the antagonist, said antagonist can also be a known compound. Therefore, before an examination with regard to said claim can be carried out the antagonist need to be specified.

- 4. In summary, the present claims are broadened in a manner that non-novel subject-matter is embraced by said claims.

 When drafting new claims, the following vague expressions should be avoided:

 The vague definition used in claim 1 item (iii) is unclear and thus objectionable under Article 6 PCT.
- 5. The applicant is informed that if the priority claimed in the present application is

International application No. PCT/US98/01774

not valid, an intermediate document becomes highly relevant for the assessment of novelty of the claims.

Inte ional Application No

| | | 101/00 30/01//1 |
|--|---|---|
| A. CLASSI IPC 6 | FICATION OF SUBJECT MATTER C12N15/12 C07K14/47 G01N | 33/50 C07K16/18 C12N5/20 |
| According to | o International Patent Classification(IPC) or to both national cla | assification and IPC |
| | SEARCHED | |
| | ocumentation searched (classification system followed by class C12N C07K G01N | sification symbols) |
| Documental | tion searched other than minimumdocumentation to the extent | that such documents are included in the fields searched |
| Electronic d | ata base consulted during the international search (name of d | lata base and, where practical, search terms used) |
| C. DOCUME | ENTS CONSIDERED TO BE RELEVANT | |
| Category ' | Citation of document, with indication, where appropriate, of t | the relevant passages Relevant to claim N |
| Р,Х | SPENCER S ET AL: "PSTPIP: a phosphorylated cleavage furrouprotein that is a substrate for tyrosine phosphatase." J CELL BIOL, AUG 25 1997, 138 UNITED STATES, XP002068211 cited in the application see the whole document WU Y ET AL: "Tyrosine phosphores." | w-associated for a PEST (4) P845-60, |
| | regulates the SH3-mediated big Wiskott-Aldrich syndrome prote PSTPIP, a cytoskeletal-associ protein." J BIOL CHEM, MAR 6 1998, 273 P5765-70, UNITED STATES, XP00 | nding of the ein to ated (10) |
| | | -/ |
| X Furti | her documents are listed in the continuation of box C. | Patent family members are listed in annex. |
| "A" docume consid "E" earlier of filling of the citation "O" docume other of the citation of t | ent defining the general state of the art which is not dered to be of particular relevance document but published on or after the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another n or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or means ent published prior to the international filing date but han the priority date claimed | "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "8" document member of the same patent family |
| Date of the | actual completion of theinternational search | Date of mailing of the international search report |
| | 6 June 1998 | 30/06/1998 |
| ivame and f | mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016 | Authorized officer Espen, J |

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Inte Ional Application No PCT/US 98/01774

| | | PC1/US 98/01//4 | | | |
|---|---|-----------------|-----------------------|--|--|
| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT Category 3 Citation of document, with indication where appropriate of the relevant passages Relevant to claim No. | | | | | |
| Category 3 | Citation of document, with indication, where appropriate, of the relevant passages | | Helevant to claim No. | | |
| X | DOSIL M ET AL: "CLONING AND CHARACTERIZATION OF FETAL LIVER PHOSPHATASE 1, A NUCLEAR PROTEIN TYROSINE PHOSPHATASE ISOLATED FROM HEMATOPOIETIC STEM CELLS" BLOOD, vol. 88, no. 12, 15 December 1996, pages 4510-4525, XP002034267 see page 4512, left-hand column | | 11 | | |
| A | GARTON A J ET AL: "IDENTIFICATION OF 130CAS AS A SUBSTRATE FOR THE CYTOSOLIC PROTEIN TYROSINE PHOSPHATASE PTP-PEST" MOLECULAR AND CELLULAR BIOLOGY, vol. 16, no. 11, November 1996, pages 6408-6418, XP002051430 cited in the application | | | | |
| A | CLOUTIER JF ET AL: "Association of inhibitory tyrosine protein kinase p50csk with protein tyrosine phosphatase PEP in T cells and other hemopoietic cells" EMBO JOURNAL, vol. 15, no. 18, 1996, EYNSHAM, OXFORD GB, pages 4909-4918, XP002068213 cited in the application | | | | |
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:

C12N 15/12, C07K 14/47, G01N 33/50, C07K 16/18, C12N 5/20

A1

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(30) Priority Data:

08/798,419 08/938.829 7 February 1997 (07.02.97) US 29 September 1997 (29.09.97) US

29 September 1997 (25.05.57)

(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application

US Filed on 08/938,829 (CIP) 29 September 1997 (29.09.97)

(71) Applicant (for all designated States except US): GENENTECH, INC. [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): LASKY, Laurence, A. [US/US]; Star Route, Box 460, Sausalito, CA 94965 (US). DOWBENKO, Donald, J. [US/US]; 456 Elm Avenue, San Bruno, CA 94066 (US).
- (74) Agents: DREGER, Ginger, R. et al.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published

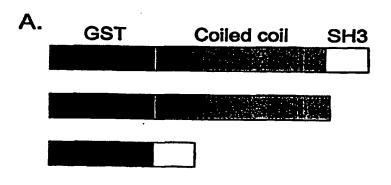
With international search report.

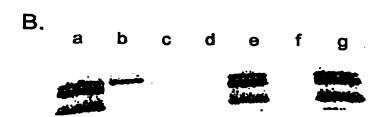
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: TYROSINE PHOSPHORYLATED CLEAVAGE FURROW-ASSOCIATED PROTEINS (PSTPIPs)

(57) Abstract

This invention concerns new PST-PIP polypeptides which are bound by and dephosphorylated by the PEST family of protein tyrosine phosphatases. The invention specifically concerns native murine PSTPIP polypeptides and their homologues in other mammals, and their functional derivatives. The invention further relates to nucleic acids encoding these proteins, vectors containing and capable of expressing such nucleic acid, and recombinant host cells transformed with such nucleic acid. Methods for inducing the polymerization of actin monomers in eukaryotic cells and assays for identifying antagonists and agonists of the PSTPIP polypeptides of the present invention are also provided.





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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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WHAT IS CLAIMED IS:

- 1.\\ An isolated PSTPIP polypeptide selected from the group consisting of:
- (i) a polypeptide comprising the amino acid sequence of the PSTPIP polypeptide shown in Rig. 1A (SEQ ID NO:1);
- (ii) a further mammalian homologue of the polypeptide of (i);
 - (iii) a polypeptide encoded by nucleic acid which hybridizes under stringent conditions to nucleic acid encoding the polypeptide of (i) or (ii) and which substantially retains the ability to bind to a member of the PEST-type protein tyrosine phosphatases; and
 - (iv) a functional derivative of any of the polypeptides (i)-(iii) substantially retaining the ability to bind to a member of the PEST-type protein tyrosine phosphatases.
- 2. The PSTPIP polypeptide of Claim 1 comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO:1).
- 3. The PSTPIP polypeptide of Claim 1 which is capable of being dephosphorylated by a member of the PEST-type protein tyrosine phosphatases when phosphorylated on at least one tyrosine residue.
- 4. The PSTPIP polypeptide of Claim 1, wherein the member of the PEST-type protein tyrosine phosphatases is PTP HSCF.
 - 5. The PSTPIP polypeptide of Claim 1 which is of murine origin.
 - 6. The PSTPIP polypeptide of Claim 1 which is of human origin.
 - 7. The PSTPIP polypeptide of Claim 1 which is devoid of a C-terminal SH3 domain.
 - 8. The PSTPIP polypeptide of Claim 1 which is not phosphorylated.
 - 9. The PSTPIP polypeptide of Claim 1 which is phosphorylated on at least one tyrosine residue.
 - 10. The PSTPIP polypeptide of Claim 1 which associates with actin.
 - 11. An antagonist of the PSTPIP polypeptide of Claim 1.
 - 12. An isolated nucleic acid sequence which encodes the PSTPIP polypeptide of Claim 1.
 - 13. A vector comprising the nucleic acid sequence of Claim 12 operably linked to control sequences recognized by a host cell transformed with the vector.
 - 14. A host cell comprising the nucleic acid sequence of Claim 12.
 - 15. A host cell comprising the vector of Claim 3.
 - 16. An antibody capable of specific binding to the PSTPIP polypeptide of Claim 1.
 - 17. The antibody of Claim 16 which is detectably beled.
 - 18. The antibody of Claim 16 which is a monoclonal antibody.
 - 19. A hybridoma cell line which produces the antibody of Claim 16.
- 20. A method for producing the PSTPIP polypeptide of Claim 1 comprising transforming a host cell with nucleic acid encoding said polypeptide, culturing the transformed cell and recovering said polypeptide from the cell culture.
 - 21. A method for inducing the polymerization of actin monomers in a eukaryotic cell comprising introducing into said cell the PSTPIP polypeptide of Claim 1.

WO 98/35037 PCT/US98/01774

22. The method of Claim 21, wherein the step of introducing comprises introducing into said cell the vector of Claim 13.

An array for identifying an antagonist or agonist of the PSTPIP polypeptide of Claim 1 which comprises contacting the PSTPIP polypeptide of Claim 1 with a candidate antagonist or agonist and monitoring the ability of said polypeptide to induce the polymerization of actin monomers.

P. .ENT COOPERATION TREA

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| ternational application No.: | Applicant's or agent's file reference: |
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| FG1/0000/01/11 | Priority date: |
| nternational filing date: | 07 February 1997 (07.02.97) |
| 30 January 1998 (30.01.98) | |
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INTERNATIONAL SEARCH REPORT

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(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference | FOR FURTHER see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. | | | | | |
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| P1066P2 | ACTION | | | | | |
| International application No. | International filing date (day/month/year) | (Earliest) Priority Date (day/month/year) | | | | |
| PCT/US 98/01774 | 30/01/1998 | 07/02/1997 | | | | |
| Applicant | | | | | | |
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| GENENTECH, INC. et al. | | | | | | |
| | n prepared by this International Searching Auth | nority and is transmitted to the applicant | | | | |
| according to Article 18. A copy is being tra | according to Article 18. A copy is being transmitted to the International Bureau. | | | | | |
| This International Search Report consists | of a total of 3 sheets. | | | | | |
| · — | of each priorart document cited in this report. | | | | | |
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| 3. X The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the | | | | | | |
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| Tran | nscribed by this Authority | | | | | |
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| 6. The figure of the drawings to be publi | shed with the abstract is: | | | | | |
| Figure No5 X as s | uggested by the applicant. | None of the figures. | | | | |
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| Category ° | Citation of document, with indication, where appropriate, of the re | elevant passages | Relevant to claim No. |
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